```
OM of: US-09-525-998A 2 to: N_Geneseq_1101:*   out_format   pfs

Date: Apr 24, 2002  9.06 AM

About: Results were produced by the GenCore software, version 4.5,
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Command line parameters:
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 -GAPEXT-4.000 -MINMATCH-0.100 -LOOPCL-0.000 -LOOPEXT=0.000
 -QGAPOP-4.500 -QGAPEXT-0.050 -XGAPOP-10.000 -XGAPEXT-0.500
 -FGAPOP-6.000 -FGAPEXT-7.000 -YGAPOP-10.000 -YGAPEXT-0.500
 -DELOP-6.000 -DELEXT-7.000 -START=1 -MATRIX=blosum62
 -TRANS-human40.cdi -LIST-45 -DOCALIGN-200 -THR_SCORE=pct
 -THR_MAX=100 -THR_MIN-0 -ALIGN-15 -MODE-LOCAL -OUTFMT-pfs
 -NORM-ext -MINLEN-0 -MAXLEN-2000000000
 -USER-US09525998_@CGN1_1_257 -NCPU-6  ICPU=3  LONGLOG -NO_XLPXY
 -WAIT -THREADS-1

Search information block:
Query: US-09-525-998A 2
Query length: 455
Database: N_Geneseq_1101:*
Database sequences: 930621
Database length: 428662619
Search time (sec): 247.030000


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seq_documentation_block:
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AC   AAQ49932;
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DT   29-APR-1994  (first entry)
XX
DE   Lambda-derived TNF-R cDNA.
XX
KW   Human; tumour necrosis factor receptor; TNF-R; interleukin-1 receptor;
KW   IL-1R; fusion protein; linker; TNF; IL-1; cachexia; cerebral malaria;
KW   rheumatoid arthritis; diabetes; multiple sclerosis; septic shock;
KW   pulmonary fibrosis; silicosis; allograft; xenograft; rejection;
KW   graft verses host disease; sepsis; inflammation; allergy;
KW   autoimmune dysfunction; ss.
XX
OS   Homo sapiens.
OS   Lambda-gt10 7-ctnfbp.
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FT   mat_peptide     121..1363
FT                   /*tag= c
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PN   WO9319777-A.
XX
PD   14-OCT-1993.
XX
PF   [illegible] MAR 1993;   [illegible]W-[illegible]02938.
XX
PR   [illegible] MAR 1992;   [illegible]205-0860710.
XX
PA   (IMMV ) IMMUNEX CORP.
XX
PI   Smith CA;
XX
DR   WPI; [illegible];
DR   P-PSDB; AAR[illegible].
XX
PT   New fusion protein tumour necrosis factor and human interleukin 1
PT   receptor - useful in therapy, diagnosis and assays of e.g.
PT   rheumatoid arthritis, diabetes, cerebral malaria, sepsis, etc.
XX
PS   Disclosure; Page 57-59; 85pp; English.
XX
CC   The sequences given in AAQ49931-32 encode human tumour necrosis factor
CC   receptor (TNF-R) and the sequences in AAQ49933-34 encode human
CC   interleukin-1 receptor (IL-1R). These sequences were used in the
CC   production of a fusion protein which conformed to one of the
CC   formulae:
CC        TNF-R-linker-TNF-R-linker-IL-1R
CC        IL-1R-linker-TNF-R-linker-TNF-R or
CC        TNF-R-linker-TNF-R
CC   The linker may comprise 5-100 amino acids selected from Gly, Asp,
CC   Ser, Thr and Ala. These linkers separate the individual moeities
CC   by such a distance that each component of the fusion protien is
CC   capable of folding into the secondary or tertiary structure required
CC   for its biological activity. These fusion proteins may be used in
CC   therapy, diagnosis and assays for conditions mediated by TNF or IL-1,
CC   particularly in conditions in which both TNF and IL-1 play a causitive
CC   role. They may be used to treat cachexia, rheumatoid arthritis,
```

```
CC   diabetes, multiple sclerosis, pulmonary fibrosis and silicosis,
CC   cerebral malaria, allograft and xenograft rejection in graft verses
CC   host disease, sepsis, septic shock, inflammation, allergies and
CC   autoimmune dysfunctions.
XX
SQ   Sequence 1368 BP; 292 A; 424 C; 376 G; 276 T; 0 other


alignment_scores:
            Quality: 2487.00              Length:    455
              Ratio:   5.466                Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-2 x AAQ49932  ..

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       1 ATGGGCCTCTCCACCGTGCCTGACCTGCTGCTGCCGCTGGTGCTCCTGGA 50

      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 GCTGTTGGTGGGAATATACCCTCAGGGGTTATTGGACTGGTCCCTCACC 100

      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 TAGGGGACAGGGAGAAGAGATAGTGTGTCCCAAGGAAAATATATC 150

      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200

      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250

      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     251 GTGACAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300

     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350

     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     351 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400

     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450

     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     451 AATGGGACCGTGCACCTCTCCTGCCAGCAGAAACAGAACACCGTGTGCAC 500

     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGIA 550

     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600

     201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650

     217 lIlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234
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     234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250
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     701 ATGGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGCAAA 750

     251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800

     267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284
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     801 GGCCCCAAACCCAGCTTCAGTCCCACTCCAGGCTTCACCCCAACCCTGG 850

     284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300
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     301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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     317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspPro 334
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTGGCTTCGACCCCA 1000

     334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050

     351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1051 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100

     367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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     384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400
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     401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250

     417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300

     434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450
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seq_documentation_block:
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AC   AAA95105;
XX
DT   12-JAN-2001  (first entry)
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DE   Human TNFR1 coding sequence.
XX
KW   TNFR1; tumour necrosis factor receptor, polymorphism, human;
KW   tumour; cancer; apoptosis; bacterial infection; ds.
XX
OS   Homo sapiens.
XX
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FT                   /*tag= c
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XX
PD   31-AUG-2000.
XX
PF   23-FEB-2000; 2000WO US04606.
XX
PR   23-FEB-1999;  99US-0121314
XX
PA   (GENA-) GENAISSANCE PHARM INC.
PA   (NAND/) NANDABALAN K.
PA   (SCHU/) SCHULZ V P.
PA   (STEP/) STEPHENS J C
PA   (CHEW/) CHEW A.
XX
PI   Nandabalan K,  Schulz VP,  Stephens JC,  Chew A;
XX
DR   WPI; 2000-543909/49.
DR   P-PSDB; AAB23446.
XX
PT   Polynucleotides comprising polymorphic variants of a reference sequence
PT   for tumour necrosis factor receptor 1 (TNFR1), useful for studying the
PT   biological function of TNFR1 and identifying drugs targeting the
PT   protein for treating disorders
XX
PS   Claim 7; Fig 4; 79pp; English.
XX
CC   The present invention relates to polymorphic variants of the tumour
CC   necrosis factor receptor 1 (TNFR1) gene. The present sequence is
CC   the coding sequence of the TNFR1 gene. The sequence of the whole gene is
CC   given in AAA95102, AAA95103 and AAA95104. The polymorphisms were
CC   identified by amplifying and sequencing regions of the gene. Twelve
CC   polymorphic loci were discovered. Of these twelve polymorphisms, four can
CC   cause a change in the TNFR1 protein. The TNFR1 polymorphisms may be
CC   useful for studying the biological function of TNFR1 as well as for
CC   identifying drugs targeting the protein for treatment of disorders
CC   related to its abnormal expression or function such as tumours,
CC   apoptosis related disorders and bacterial infection.
XX
SQ   Sequence 1368 BP; 292 A; 424 C; 276 G; 276 T; 0 Other;


alignment_scores:
            Quality: 2487.00              Length:    455
              Ratio: 5.466                  Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-2 x AAA95105

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       1 ATGGGCCTCTCCACCGTGCCTGACCTGCTGCTCCCGCTGGTCCTGCTGGA 50

      47 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 94
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 GCTGTTGGTGGGAATATACCCTCAGGGCTTATTGGACTGGTCCCTCACC 100

      94 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 TAGGGGACAGGGAGAAGAGAGATAGTGTGTGCCCAAGGAAAATATATC 150

      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 97
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200

      97 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     201 CTTGTACAATGACTGTCCAGGCCCGGGCCAGGATACGGACTGCAGGGAGT 250

      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 106
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     251 GTGAGAGCGGCTCTTTCACAGCTTCAGAAAACACACTCAGACACTGCCTC 400

     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 450

     117 sThrValAspArgAspThrValCysGlyAlaArgLysAsnGlnTyrArgH 134
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     351 CACAGTGCACCGGCACACCGTGTGTGGCTGCAGCAACAACCAGTACCGGC 400

     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167
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 284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300
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 301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317
     ||||||||||||||||||||||||||||||||||||||||||||||||||||
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 317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334
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 351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367
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 401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417
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seq_documentation_block:
ID   AAQ20973 standard; DNA; 2062 BP.
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AC   AAQ20973;
XX
DT   11-MAY-1992  (first entry)
XX
DE   TNF-alpha binding protein gene.
XX
KW   Tumour necrosis factor alpha, autoimmune diseases, cachectin; ss;
KW   extracellular domain.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
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FT                   /note= "encodes the extracellular domain of human
FT                         TNF alpha receptor"
XX
PN   GB2246569-A.
XX
PD   05-FEB-1992.
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PF   15-JUN-1990;   90GB-0013410.
XX
PR   15-JUN-1990;   90GB-0013410.
XX
PA   (CHAR-) CHARING CROSS SUNLE.
XX
PI   Feldman M,  Gray P,  Turner M,  Brennan F;
XX
DR   WPI; 1992-043613/06.
DR   P-PSDB; AAR20787.
XX
PT   New tumour necrosis factor alpha binding protein and polypeptide
PT   - useful in treating cachexia, sepsis and auto immune diseases
PT   e.g. rheumatoid arthritis
XX
PS   Disclosure; Fig 1; 25pp; English.
XX
CC   The sequence is that of DNA encoding tumour necrosis factor alpha
CC   binding protein which was obtd. from a human placental cDNA library
CC   in lambda gt11 using a probe (AAQ20974). The DNA also encodes the
CC   extracellular domain of human TNF alpha receptor and as such it is
CC   useful for treating diseases where TNF alpha is involved as a
CC   causative agent, e.g. cachexia, sepsis and autoimmune diseases,
CC   specifically rheumatoid arthritis. See also AAQ20974.
XX
SQ   Sequence 2062 BP; 429 A, 616 C, 573 G, 444 T, 0 other;


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            Quality: 2487.00              Length:    455
              Ratio:  5.466                 Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

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seq_documentation_block:
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AC AAQ24440;
XX
DT 05-NOV-1992 (first entry)
XX
DE Encodes TNF-alpha 55kD receptor.
XX
KW tumour necrosis factor alpha, extracellular binding domain;
KW treatment, pulmonary diseases, septic shock, HIV infection; AIDS;
KW malaria; viral meningits; graft versus host disease;
KW autoimmune disease; rheumatoid arthritis.
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OS Homo sapiens.
XX
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PN WO9207076-A.
XX
PD 30-APR-1992.
XX
PF 18-OCT-1991; 91WO-GB01826.
XX
PR 18-OCT-1990; 90GB-0022648.
XX

PA (CHAR-) CHARING CROSS SUNLEY RES CENT.
XX
PI Brennan FM, Feldmann M, Gray PW, Turner MJC;
XX
DR WPI; 1992-167156/20.
DR P-PSDB; AAR24000.
XX
PT New polypeptide capable of binding human TNF alpha - comprises
PT first three cysteine-rich subdomains of TNF alpha receptor for
PT treating autoimmune disease, septic shock, HIV etc.
XX
PS Claim 4; Fig 1; 43pp; English.
XX
CC This sequence encodes human TNF alpha 55kD receptor . A placenta cDNA
CC library in gt10 was screened with probe AAQ29236. Ten hybridising clones
CC were plaque purified and cDNA size determined by PAGE against an
CC Eco RI digested phage DNA. The inserts of two cDNA clones were then
CC sequenced The coding region of the majority of the human TNF-alpha
CC 55kD receptor was isolated as an EcoRI fragment encoding 374 amino
CC acids, and cloned into a mammalian cell expression vector, resulting
CC in prTNFR. A derivative of the TNF alpha receptor was produced by
CC engineering a termination codon just prior to the transmembrane
CC domain. PCR with primers AAQ29237,8 generated a 300bp
CC restriction fragment which was cloned into prTNFR, giving pTNFRecd.
CC DNA sequencing confirmed this contained the designed DNA sequence.
CC The TNF-alpha receptor expression plasmids were then transfected
CC into monkey COS-7 cells.
CC See also AAQ24440-51, AAR24000, AAR24080-84, AAR27585, AAQ29236-8
XX
SQ Sequence 2062 BP; 429 A; 618 C; 572 G; 443 T; 0 other;

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Ratio: 5.466 Gaps: 0
Percent Similarity: 100.000 Percent Identity: 100.000

alignment_block:
US-09-525-998A-2 x AAQ24440 ..

Align seq 1/1 to: AAQ24440 from: 1 to: 2062

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     17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34
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    134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150
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    167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184
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DT   13-MAY-1991  (first entry)
XX
DE   30kD TNF inhibitor precursor gene in lambda-gt10-7ctnfbp.
XX
KW   Tumour necrosis factor; inhibitor; ss.
XX
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XX
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PN   AU9058976-A.
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PD   24-JAN-1991.
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PF   16-JUL-1990;   90AU-0058976.
XX
PR   07-FEB-1990;   90US-0479661.
PR   18-JUL-1989;   89US-0381080.
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XX
PA   (SYNE-) SYNERGEN INC.
XX
DR   WPI; 1991-073847/11
DR   P-PSDB; AAR10986.
XX
PT   Tumour necrosis factor inhibitor - for suppression of TNF-alpha
PT   and -beta, useful as therapeutic agent.
XX
PS   Disclosure; Fig 21; 142pp; English.
XX
CC   The sequence encodes the entire 30 kD TNF inhibitor. The clone from
CC   which the sequence was obtd. was isolated from a cDNA library
CC   prepd. from RNA form U937 cells treated with PMA/PHA.   The whole
CC   gene can be inserted into expression vectors for prepn. of TNF
CC   inhibitor for use in the treatment of inflammatory and degenerative
CC   diseases.
CC   See also AAQ10878, AAQ10884 and AAQ10907.
XX
SQ   Sequence 2088 BP; 439 A; 626 C; 578 G; 445 T; 0 other;


alignment_scores:
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         ||||||||||||||||||||||||||||||||||||||||||||||||||
     969 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 1018

     284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1019 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 1068

     301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1069 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 1118

     317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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     1119 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1168

      434 lePro AsnPro LeuGln LysTrp GluAsp SerAla His LysPro GlnSer 350
          |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
     1169 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1218

      351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367
          |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
     1219 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1268

      367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384
          |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
     1269 CCCGTTGCGCTGGAACGAATTCGTGCGGCGCCCTAGGGCTGAGCGACCACG 1318

      384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400
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     1319 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1368

      401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417
          |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
     1369 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1418

      417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434
          |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
     1419 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1468

      434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450
          |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
     1469 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1518

      451 ProSerLeuLeuArg 455
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     1519 CCCAGTCTTCTCAGA 1533

seq_name: /SIDS2/qcqdata/geneseq/geneseqn/NA2001.DAT:AAC83946

seq_documentation_block:
ID   AAC83946 standard; DNA; 2088 BP
XX
AC   AAC83946;
XX
DT   02-MAR-2001  (first entry)
XX
DE   Human 30 kDa TNF inhibitor precursor coding sequence.
XX
KW   TNF inhibitor; antiinflammatory; Tumour Necrosis Factor, interleukin,
KW   IL-1; inflammatory disease; degenerative disease; human; ss.
XX
OS   Homo sapiens.
XX
PN   US6143866-A.
XX
PD   07-NOV-2000.
XX
PF   19-JAN-1995;   95US-0375242.
XX
PR   19-JUL-1990;   90US-0555274.
PR   09-JUL-1993;   93US-0090466.
PR   18-JUL-1989;   89US-0381080.
PR   11-DEC-1989;   89US-0450329.
PR   07-FEB-1990;   90US-0479661.
XX
PA   (AMGE-) AMGEN INC.
XX
PI   Squires C,  King MW,  Hale KK,  Brewer MT,  Thompson RC;
PI   Vanderslice KW,  Vannice J,  Kohno T,
XX
DR   WPI; 2001-006443/01.
DR   P-PSDB; AAB37677.
XX
PT   Novel 30 kDa tumor necrosis factor inhibitor analog comprising a
PT   non-native cysteine residue cross-linked with polyethylene glycol,
PT   useful for treating inflammatory and degenerative diseases mediated by
PT   TNF.
XX
PS   Example 6; Fig 21; 82pp; English.
XX
CC   The present invention relates to Tumour Necrosis Factor (TNF) inhibitors
CC   (see AAB37676 and AAB37685), which have TNF inhibitory activity. The
CC   novel TNF inhibitors of the present invention are useful as therapeutic
CC   agents for inhibiting the activity of TNF and interleukin (IL-1), and
CC   for treating inflammatory and degenerative diseases mediated by TNF. The
CC   present sequence is the coding sequence for the precursor of 30 kDa TNF
CC   inhibitor. The 30 kDa INF inhibitor can inhibit TNF alpha.
XX
SQ   Sequence 2088 BP; 439 A; 626 C; 578 G; 445 T; 0 other;


alignment_scores:
            Quality: 2487.00              Length:    455
              Ratio:  5.466                 Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-2 x AAC83946   ..

 Align seq 1/1  to: AAC83946  from: 1  to: 2088

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       17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34
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      219 GCTGTTGGTGGGAATATACCCTCAGGGGTTATTGGACTGGTCCCTCACC 268

       34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50
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      269 TACGGCACAGGGAGAAGAGACATAGTGTGTGTCCCCAAGCAAAATATATC 318

       51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67
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      319 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 368

       67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      369 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 418

       84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      419 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCACACACTGCCTC 468

      101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      469 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 518

      117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      519 CACACTGGACCCGCACACGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 568

      134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      569 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 618

      151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      619 AATGGGACCGTGCACCTTTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 668

      167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184
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      669 CTGCCATGCAGGTTTCTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 718

      184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200
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    217 IlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234
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    919 TCCACACCTGAAAAAGAGGGGCAGCTTGGAAGCAACTACTACTAAGCCCCT 968

    267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284
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    969 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 1018

    284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300
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   1019 GCTTCAGTCCCCTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 1068

    301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317
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    317 oTyrGlnGlyAlaAspPro[illegible]LeuAlaThrAlaLeuAlaSerAspPro[ 331
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    334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350
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   1169 TCCCCAACCCCCTTCAAAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1218

    351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367
        ||||||||||||||||||||||||||||||||||||||||||||||||||
   1219 CTAGACACTGATGACCCCGCGACCCTGTACGCCGTGGTGGAGAACGTGCC 1268

    367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384
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   1269 CCGTTGCGGTGGAAGGAATTCGTGCGGCGGCTAGGGCTGAGCGACCACG 1318

    384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400
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   1319 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1368

    401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417
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    417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434
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   1419 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1468

    434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450
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   1469 TGCAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCCCG 1518

    451 ProSerLeuLeuArg 455
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   1519 CCCAGCTCTTCTCAGA 1533

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ID   AA209170 standard; cDNA; 2111 BP.
XX
AC   AA209170;
XX
DT   18-OCT-1999  (first entry)
XX
DE   Human tumour necrosis factor binding protein 1 DNA.
XX
KW   Tumour necrosis factor binding protein; TNF; insoluble protein; agonist;
KW   anti-inflammatory; antimalarial; treatment; septic shock; inflammation;
KW   autoimmune glomerulonephritis; cerebral malaria; immune response;
KW   antagonist; diagnosis; ds.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   CDS             187..1554
FT                   /*tag= a
FT                   /product= "TNF binding protein"
FT   sig_peptide     187..273
FT                   /*tag= b
FT   mat_peptide     274..1551
FT                   /*tag= c
XX
PN   EP939121-A2.
XX
PD   01-SEP-1999.
XX
PF   31-AUG-1999;    99EP-0116707.
XX
PR   20-APR-1990;    90CH-0001347.
PR   12-SEP-1989;    89CH-0003319.
PR   08-MAR-1999;    99CH-0000746.
XX
PA   (BOEH ) BOEHRINGER GA KOCHE & CO AG F.
XX
PI   Brockhaus M.  Lesslauer W.  Loetscher H;
PI   Schlaeger E;
XX
DR   WPI; 1999-480840/41.
DR   P-PSDB; AAY30944.
XX
PT   New insoluble proteins, and fragments, that bind to tumor necrosis
PT   factor, used to treat e.g. septic shock or cerebral malaria
XX
PS   Claim 4; Fig 1; 25pp; German.
XX
CC   This invention describes novel homogeneous insoluble proteins (I),
CC   their (in)soluble fragments (Ia) and their salts that can bind tumour
CC   necrosis factor (TNF). The products of the invention have
CC   anti inflammatory and antimalarial activity. (I) and (Ia) are used (i)
CC   to treat diseases in which TNF is involved (e.g. septic shock, autoimmune
CC   glomerulonephritis, cerebral malaria, immune responses and inflammation),
CC   (ii) to purify TNF, (iii) to identify TNF (antagonists and (iv) for
CC   diagnostic determination of TNF in body fluids. Antibodies raised against
CC   (I) are used for affinity purification of (I). This sequence encodes
CC   a tumour necrosis factor binding protein described in the method of
CC   the invention.
XX
SQ   Sequence 2111 BP; 445 A; 629 C; 587 G; 450 T; 0 other;


alignment_scores:
            Quality: 2487.00              Length:    455
              Ratio:   5.466                Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-2 x AA209170   ..

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     187 ATGGGCCTCTCCACCGTGCCTGACCTGCTGCTGCCGCTGGTGCTCCTGGA 236

      17 GLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 64
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     237 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGACTGGTCCCTCACC 286
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 34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50
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287 TAGGGCACAGGACAACAGACATAGTGTGTCTCCCAAGGAAAATATATC 336

 51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67
    ||||||||||||||||||||||||||||||||||||||||||||||||||
337 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 386

 67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84
    ||||||||||||||||||||||||||||||||||||||||||||||||||
387 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 436

 84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100
    ||||||||||||||||||||||||||||||||||||||||||||||||||
437 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 486

101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117
    ||||||||||||||||||||||||||||||||||||||||||||||||||
487 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 536

117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134
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537 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACGGC 586

134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150
    ||||||||||||||||||||||||||||||||||||||||||||||||||
587 ATTATTGGAGTGAAAACCTTTTCCACTGCTTCAATTGCAGCCTCTGCCTC 636

151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167
    ||||||||||||||||||||||||||||||||||||||||||||||||||
637 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 686

167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184
    ||||||||||||||||||||||||||||||||||||||||||||||||||
687 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 736

184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200
    ||||||||||||||||||||||||||||||||||||||||||||||||||
737 ACTGTAAGAAAAGCCTGGAGCTGCACCAAGTTGTGCCTACCCCAGATTGAG 786

201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217
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787 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 836

217 lIlePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234
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837 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 886

234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250
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887 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 936

251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267
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937 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 986

267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284
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987 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 1036

284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300
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1037 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 1086

301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317
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1087 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 1136

317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334
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334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350
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1187 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1236

351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367
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1237 CTAGACACTGATGACCCGGCAACGCTGTACGCCGTGGTGGAGAACGTGCC 1286

367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384
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1287 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1336

384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400
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1337 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1386

401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417
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1387 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGGAGGCCAC 1436

417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434
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1437 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1486

434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450
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1487 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1536

451 ProSerLeuLeuArg 455
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seq_documentation_block:

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ID   AAZ48475 standard; DNA; 2161 BP.
XX
AC   AAZ48475;
XX
DT   31-MAR-2000  (first entry)
XX
DE   Human tumour necrosis factor receptor (TNFR1) nucleotide sequence.
XX
KW   Tumour necrosis factor receptor type 1; TNFR1; antisense; infection;
KW   inflammation; tumour formation; TNFR1; anticancer; ds.
XX
OS   Homo sapiens.
XX
PN   US6007995-A.
XX
PD   28-DEC-1999.
XX
PF   26-JUN-1998;   98US-0106038.
XX
PR   26-JUN-1998;   98US-0106038.
XX
PA   (ISIS-) ISIS PHARM INC.
XX
PI   Baker BF,  Cowsert LM;
XX
DR   WPI; 2000-105333/09.
XX
PT   Antisense inhibition of tumor necrosis factor type 1 expression for
PT   diagnosis, treatment and prevention of disease, particularly tumors
XX
PS   Example 10; Columns 33-36; 34pp; English.
XX
CC   The invention provides antisense compounds targeted to human tumour
CC   necrosis factor receptor type 1 (TNFR1) RNA. These antisense compounds
CC   can be used in a method of inhibiting the expression of TNFR1 human cells
CC   or tissues. The antisense compounds specifically hybridize with one or
CC   more nucleic acids encoding TNFR1 modulating the function of nucleic
CC   acid molecules encoding TNFR1, ultimately modulating the amount of TNFR1
```

```
CC   produced. The antisense compounds and method are useful as research
CC   reagents and diagnostics, and in the treatment and prophylaxis of
CC   infection, inflammation or tumour formation. The present sequence
CC   represents the nucleotide sequence of human TNFR1 (GenBank Accn No:
CC   X55313).
XX
SQ   Sequence 2161 BP; 459 A; 642 C; 604 G; 456 T; 0 other;


alignment_scores:
            Quality: 2487.00              Length:    455
              Ratio:  5.466                 Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-2 x AA248475   ..

 Align seq 1/1  to: AA248475  from: 1  to: 2161

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      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     306 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGACTGGTCCCTCACC 355

      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     356 TAGGGCACAGGGACAAGACAGATAGTGTGTGTCCCCAAGGAAAATATATC 405

      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     406 CACCCTCAAAATAATTCGATTGCTGTATGTAAGTGCCACAAAGGAACCTA 455

      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84
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      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100
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     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134
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     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150
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     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167
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     217 lIlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234
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seq_documentation_block:
ID   AAQ90513 standard; DNA; 2175 BP
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AC   AAQ90513;
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DT   19-JAN-1996  (first entry)
XX
DE   p55 TNF-R gene.
XX
KW   p55; tumour necrosis factor receptor; TNF-R; human; murine; chimera;
KW   epidermal growth factor receptor; EGF-R; protease inhibitor;
KW   phorbol myristate acetate; PMA; ss.
XX
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FT   misc_signal     2143..2149
FT                   /*tag= b
FT                   /note= "possible poly-A signal"
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PN   AU9475742-A.
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PD   04-MAY-1995.
XX
PF   11-OCT-1994;   94AU-0075742.
XX
PR   12-OCT-1993;   93IL-0107268.
XX
PA   (YEDA ) YEDA RES & DEV CO LTD.
XX
PI   Batkin M,  Brakebusch C,  Varfolomeev E,  Wallach D;
XX
DR   WPI; 1995-194342/26.
DR   P-PSDB; AAR75084.
XX
PT   New protease capable of cleaving soluble tumour necrosis factor
PT   (TNF) receptor - from cell-bound TNF receptor, useful for
PT   antagonising deleterious effects of TNF.
XX
PS   Disclosure; Fig 1, 40pp; English.
XX
CC   This sequence represents human p55 tumour necrosis factor (TNF-R) DNA.
CC   Expression of this receptor is regulated by shedding of the
CC   extracellular receptor fragment. The p55 TNF-R can be shed in response
CC   to different inducing agents, e.g. phorbol myristate acetate (PMA),
CC   depending on cell type. The only region of the receptor whose structure
CC   affects the shedding response is the spacer region (see AAR75012) in the
CC   extracellular domain. This region is located close to a site of cleavage
CC   of the molecule, and links the Cys rich module to the transmembrane
CC   domain. The spacer region of the encoded protein was used to create the
CC   chimeras between human p55 TNF-R and murine epidermal growth factor
CC   receptor (EGF-R) that are represented by AAR75007-11. This spacer region
CC   was subjected to deletion mutations (AAR75013-25) and substitutions
CC   (AAR75026-47). Of the spacer region, the most important residues are
CC   Asn 172, Val 173, Lys 174 and Gly 175, with Val 173 being the most
CC   important of these. The shedding of the receptor is independent of the
CC   side chain identity of these residues, with the exception of a limited
CC   dependence on the identity of Val 173. Mutations which alter the
CC   conformation of the protein adversely effect the shedding process. The
CC   mutations shown in AAR75013-47 were introduced in order to create an
CC   inhibitor of a protease that is capable of cleaving the soluble TNF-R
CC   from the cell bound TNF-R. Fragments of these inhibitors can be seen in
CC   AAR75017-9, AAR75025, AAR75033-5 and AAR75042-3. These protease
CC   inhibitors can be used for enhancing TNF function.
XX
SQ   Sequence 2175 BP; 474 A; 642 C; 603 G; 456 T; 0 other;


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              Ratio:  5.466                 Gaps:      0
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seq_documentation_block:
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AC   AAQ10955;
XX
DT   24-MAY-1991  (first entry)
XX
DE   Encodes human 55kD TNF-binding protein.
XX
KW   Tumour Necrosis Factor, binding proteins, septic shock;
KW   autoimmune glomerulonephritis; lymphokine; cytokine.
XX
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PF   31-AUG-1990;   90EP-0116707.
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PI   Schlaeger EJ;
XX
DR   WPI; 1991-081951/12.
DR   P-PSDB; AAR11082.
XX
PT   Insoluble tumour necrosis factor binding proteins and DNA
PT   encoding them, useful in pharmaceutical prods. and for antibody
PT   prodn.
XX
PS   Claim 4; Fig 1; 26pp; German.
XX
CC   Partial amino acid sequences were determined for the 55 and 75kD
CC   TNF-BPs (see AAR11072-R11081) and oligonucleotide primers were
CC   synthesised based on these partial sequences. The primers were used
CC   to produce a cDNA fragment for use as aprobe to screen a human
CC   placental cDNA bank constructed in lambda gt11. Positive clones were
CC   identified and sequenced. DNA constructs comprising the TNF-BP coding
CC   sequence ma; also contain a fragment encoding a human Ig domain.
CC   Recombinant constructs are used to transform cells to confer
CC   improved TNF binding properties.
CC   See also AAQ10956.
XX
SQ   Sequence 2111 BP; 445 A; 628 C; 588 G; 450 T; 0 other;


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```

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 201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217
     ||||||||||||||||||||||||||||||||||||||||||||||||||
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 351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1237 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1286

 367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1287 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1336

 384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1337 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1386

 401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1387 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1436

 417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434
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1437 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1486

 434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450
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seq_name: [illegible] AAQ50870

seq_documentation_block:

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ID   AAQ50870 standard; DNA; 2170 BP.
XX
AC   AAQ50870;
XX
DT   13-MAY-1994  (first entry)
XX
DE   p55 Tumour necrosis factor receptor coding sequence.
XX
KW   TNF; tumour necrosis factor, receptor, disease, autoimmunity;
KW   rheumatoid arthritis; graft rejection; graft vs. host; septic shock;
KW   effector protein, ss.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   CDS             256..1623
FT                   /*tag= a
FT                   /product= p55 Tumour necrosis factor receptor.
XX
PN   EP568925-A.
XX
PD   10-NOV-1993.
XX
PF   29-APR-1993;   93EP-0106981.
XX
PR   03-MAY-1992;   92IL-0101769.
XX
PA   (YEDA ) YEDA RES & DEV CO LTD.
XX
PI   Brakebusch C,  Wallach D;
XX
DR   WPI; 1993-353057/45.
DR   P-PSDB; AAR42197.
XX
PT   Modulating activity of tumour necrosis factor receptor - using
PT   peptide(s), antibodies, etc. which interact with critical regions
PT   of receptor or effector protein, for controlling auto immune
PT   disease, septic shock, etc.
XX
PS   Claim 2; Figure 1; 17pp; English.
XX
CC   Modification of the tumour necrosis factor receptor by mutation or
CC   deletion modulates signal transduction and/or cleavage effected by
CC   the receptor.  This modulation of activity can also be achieved
CC   using effector proteins which interact with the TNF receptor.
CC   Molecules which interact with the TNF receptor or the effector
CC   proteins can be used to treat or prevent diseases associated with
CC   TNF activity e.g. autoimmune disease; rheumatoid arthritis; graft
CC   rejection, graft vs. host disease or septic shock.  They can also
CC   be used to treat overdoses of exogenous TNF.
XX
SQ   Sequence 2170 BP; 474 A; 657 C; 584 G; 455 T; 0 other;
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alignment_scores:
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             Ratio:   5.446                Gaps:       0
 Percent Similarity: 100.000   Percent Identity: 99.560

alignment_block:
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      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34
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     306 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGACTGGTCCCTCACC 355

      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50
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  51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67
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 406 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 455

  67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84
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 456 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 505

  84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100
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 101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117
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 556 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 605

 117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134
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 606 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 655

 134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150
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 184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200
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 201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217
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 856 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 905

 217 IlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234
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 234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250
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 251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267
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 267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284
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 384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400
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 401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417
     ||||||||||||| ||||||||||||||||||||||||||||||||||||
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     ||||||||||||||||||||||||||||||||||||||||||||||||||
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 434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450
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1556 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1605

 451 ProSerLeuLeuArg 455
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seq_name: [illegible] AAQ06285

seq_documentation_block:

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ID   AAQ06285 standard; DNA; 2141 BP.
XX
AC   AAQ06285;
XX
DT   29-JAN-1991  (first entry)
XX
DE   Human Tumour Necrosis factor Receptor cDNA insert.
XX
KW   Tumour necrosis factor binding protein; TNF BP; TNF-receptor;
KW   lambdaTNF-R2; raTNF-R8; ss.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   CDS             213..1577
FT                   /*tag-  a
FT                   /label-huTNF-R
XX
PN   EP393438-A.
XX
PD   24-OCT-1990.
XX
PF   06-APR-1990;   90EP-0106624.
XX
PR   21-JUN-1989;   89DE-3920282.
PR   21-APR-1989;   89DE-3913101.
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PA   (BOEH ) BOEHRINGER INGELHEIMINT.
XX
PI   Hauptmann R,  Himmler A,  Maurer-Fogy I,  Stratowa C;
XX
DR   WPI; 1990-321987/43.
DR   P-PSDB; AAR07451.
XX
PT   DNA encoding TNF binding protein and TNF  receptor - used in
PT   tumour treatment and to understand mechanismsm to TNF action
XX
PS   Disclosure; Fig 91(1-2); 51pp; German.
XX
CC   raTNF-R8 (AAQ06284) was used to screen the HS913T cDNA library.
CC   LambdaTNF-R2 encodes the complete human TNF R2 and was used to
```

```
CC   construct a plasmid (pADTNF-R) expressing the product the same way
CC   as pADTNF-BP (see AAQ06282).
CC   See also AAQ06282-Q06285.
XX
SQ   Sequence 2141 BP; 455 A; 633 C; 593 G; 460 T; 0 other;


alignment_scores:
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              Ratio:  5.431                 Gaps:       0
 Percent Similarity: 100.000   Percent Identity:  94.321

alignment_block:
 US-09-525-998A-2 x AAQ06285   ..

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      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34
         ||||||||||||||||||||||||:::||||||||||||||||||||||
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         ||||||||||||||||||||||||||||||||||||||||||||||||||
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      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84
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      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100
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     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134
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     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167
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     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184
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Seq_name: /SIDS2/qcgdata/geneseq/geneseqn/NA1991.DAT:AAQ12215

seq_documentation_block:
ID   AAQ12215 standard; DNA; 2176 BP.
XX
AC   AAQ12215;
XX
DT   12-SEP-1991  (first entry)
XX
DE   Type I TNF receptor.
XX
KW   Tumour Necrosis Factor; TNF; binding protein; TBP-I; ss.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   terminator      244..246
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FT   mat_peptide     319..1620
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FT                   /label= soluble_domain
FT                   /note= "may be 2 codons shorter or a few codons
FT                    longer"
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FT   misc_feature    850..858
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XX
PF   13-DEC-1990;   90EP-0124133.
XX
PR   12-JUL-1990;   90IL-0095064.
PR   13-DEC-1989;   89IL-0092697.
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PA   (YEDA ) YEDA RES & DEV CO LTD.
XX
PI   Wallach D,  Nophar Y,  Kemper O,  Engelmann H,  Brakebusch C;
PI   Aderka D;
XX
DR   WPI; 1991-186774/26.
DR   P-PSDB; AAK12550.
XX
PT   Recombinant tumour necrosis factor binding protein I  prepd  by
PT   transfecting eukaryotic cells with vector contg. deoxyribonucleic
PT   acid encoding human type I TNF receptor or soluble domain
XX
PS   Disclosure; Fig 1(D); 30pp; English.
XX
CC   The Tumour Necrosis Factor Binding Protein I is the soluble form of
CC   type I TNF-receptor and constitutes a fragment of the cell surface
CC   form of this receptor, corresp. to its extracellular domain.
CC   There is no characteristic poly(A) addition signal near the 3' end
CC   of the cDNA.  The sequence ACTAAA (tag m) may serve as an
CC   alternative to this signal, but with low efficiency.
CC   See also AAQ12212-15.
XX
SQ   Sequence 2176 BP; 475 A; 644 C; 602 G; 455 T; 0 other;
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            Quality: 2464.00              Length:    455
              Ratio:  5.439               Gaps:        0
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alignment_block:
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      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34
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      51 HisProGluAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67
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      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     456 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 505

      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100
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     506 CTGAGAGCGGCTCCTTCACCGCTGAGAAACACCTCCGAGACACTGCCTC 555

     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117
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     556 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 605

     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134
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    367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384
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    417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434
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seq_documentation_block:
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AC   AAQ06282;
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DT   29-JAN-1991  (first entry)
XX
DE   Plasmid Tumour Necrosis Factor-Binding Protein 15 cDNA insert.
XX
KW   Tumour necrosis factor binding protein; TNF-BP; TNF-receptor;
KW   pTNF-BP15; ss.
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PN   EP393438-A.
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PD   24-OCT-1990.
XX
PF   06-APR-1990;    90EP-0106624.
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PR   21-JUN-1989;    89DE-3920282.
PR   21-APR-1989;    89DE-3913101.
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PA   (BOEH ) BOEHRINGER INGELHEIMINT.
XX
PI   Hauptmann R,  Himmler A,  Maurer-Fogy I,  Stratowa C;
XX
DR   WPI; 1990-321987/43.
DR   P-PSDB; AAR07449.
XX
PT   DNA encoding TNF binding protein and TNF receptor - used in
PT   tumour treatment and to understand mechanismsm to TNF action
XX
PS   Disclosure, Fig 1(1-3), 51pp; German.
XX
CC   pTNF-BP15 is one of 30 positives clones in a screened cDNA library
CC   from induced TNF-induced fibrosarcoma cells.  A TNF-BP had been
CC   isolated from the urine of patients with uraemia and probes/primers
CC   were constructed from the determined amino acid sequence.
CC   To produce a vector expressing a soluble form of TNF-binding
CC   protein, this plasmid was cut with XmnI, amplified by PCR and the
CC   amplified DNA cut with BamHI and EcoRI.
CC   The resulting 0.75 kb DNA fragment was inserted into pT7/T3 alpha-19
CC   (BRL) cut with the same enzymes to recover pTNF-BP.  This was cut
CC   with BamHI and EcoRI, and the recovered fragment inserted into
CC   pAD-CMV1 (AAQ06283) to give the required plasmid pADTNF-BP.
CC   See also AAQ06282 Q06285.
XX
SQ   Sequence 1334 BP; 299 A; 409 C; 342 G; 284 T; 0 other;


alignment_scores:
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        ||||||||||||||||||||||||||||||||||||||||||||||||||
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    217 IlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234
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seq_documentation_block:
ID   AAQ06284 standard; DNA; 2173 BP.
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AC   AAQ06284;
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DT   29-JAN-1991  (first entry)
XX
DE   Rat tumour Necrosis Factor Receptor 8 cDNA.
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KW   Tumour necrosis factor binding protein; TNF BP; TNF-receptor;
KW   raTNF-R8; ss.
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PN   EP393438 A.
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PD   24-OCT-1990.
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PF   06 Apr 1990;    90EP-0106024.
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PR   21-JUN-1989;    89DE-3920282.
PR   21-APR-1989;    89DE-3913101.
XX
PA   (BOEH ) BOEHRINGER INGELHEIMINT.
XX
PI   Hauptmann R, Himmler A, Maurer-Fogy I, Stratowa C;
XX
DR   WPI: 1990-321987/43.
DR   P-PSDB; AAP07450.
XX
PT   DNA encoding TNF binding protein and TNF- receptor - used in
PT   tumour treatment and to understand mechanismsm to TNF action
XX
PS   Disclosure; Fig 8(1-2); 51pp; German.
XX
CC   A rat brain cDNA analogue of the HS913T cDNA library from rat
CC   glioma cell line C6 (ATCC CCL107) is prepared in lambda gtll.
CC   The isolated clone ratNF-R8 is used as probe to isolated the entire
CC   human TNF receptor, as represented in AAQ06285.
CC   See also AAQ06282-Q06285.
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SQ   Sequence 2173 BP; 503 A, 642 C, 551 G, 477 T; 0 other;


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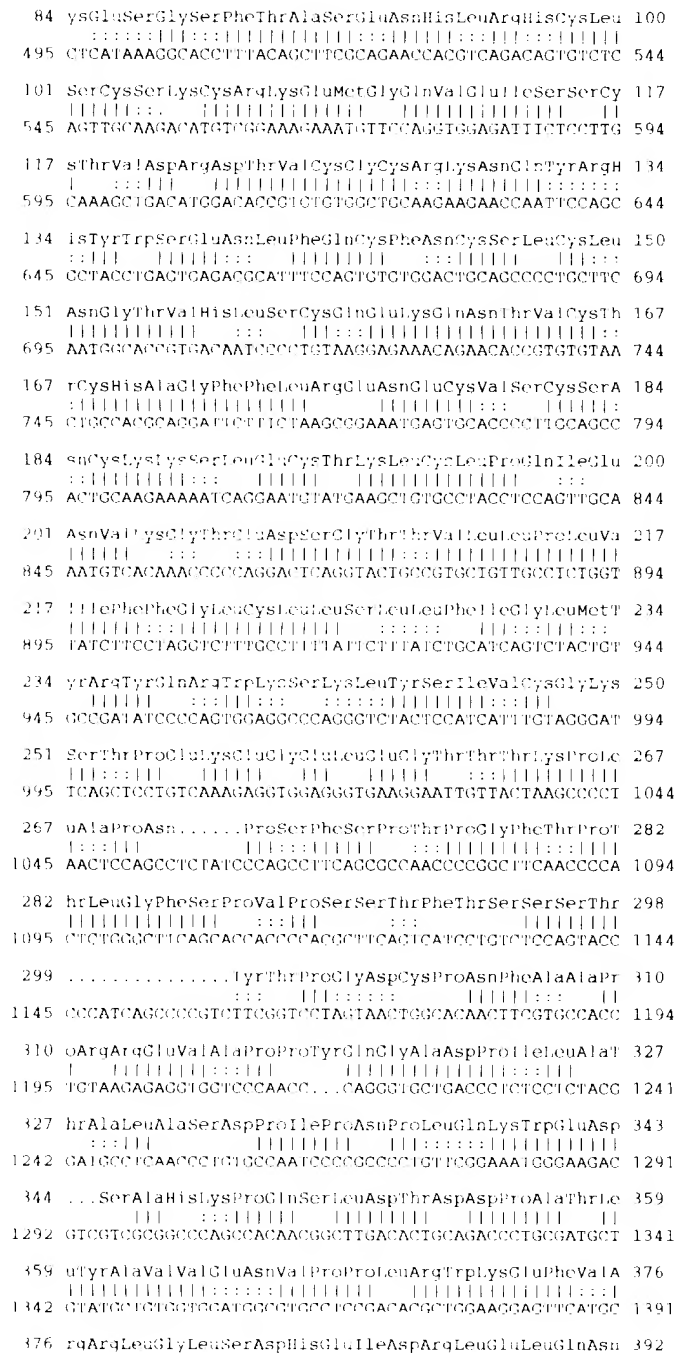
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